Hydroxychloroquine Screening Practice Patterns Within a Large Multispecialty Ophthalmic Practice

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• PURPOSE: To determine provider compliance with hydroxychloroquine screening following the revised recommendations published in 2011 by the American Academy of Ophthalmology.

• DESIGN: Evaluation of adherence to a screening protocol.

• METHODS: Subjects were identified with hydroxychloroquine as a medication by electronic query at a large multispecialty ophthalmic practice. Patients were excluded if patients: (1) were screened by an outside physician; (2) lacked recorded height, weight, start date, or dosing; or (3) took hydroxychloroquine for malaria prophylaxis. Screening tests were stratified by ophthalmic subspecialty. Guidelines define proper screening as 1 subjective test—Humphrey visual field (HVF), and 1 objective test—spectral-domain optical coherence tomography (SD OCT), fundus autofluorescence (FAF), or multifocal electroretinography (mfERG). Adherence to guidelines was determined by categorizing practices as: (1) "appropriate"—consistent with guidelines; (2) "underscreened"—insufficient testing; or (3) "inappropriate"—no testing.

• RESULTS: The study comprised 756 patients with a mean age of 56 years undergoing 1294 screening visits. Twenty-one patients received initial screenings outside the institution. Most common screening tests employed included SD OCT (56.6%), 10-2 HVF (55.0%), and Amsler grid (40.0%). Of the 735 initial screenings, 341 (46.4%) were appropriately screened, 204 (27.8%) underscreened, and 190 (25.9%) inappropriately screened. Of those who presented solely for screening (560), 307 (54.8%) were appropriately screened, 144 (25.7%) underscreened, and 109 (19.5%) inappropriately screened.

• CONCLUSIONS: Of patients presenting for hydroxychloroquine screening, 54.8% of patients received appropriate evaluation, indicating lack of adherence to guidelines. Overall, SD OCT and 10-2 HVF were the preferred screening modalities, with FAF and mfERG less frequently ordered. (Am J Ophthalmol 2015;160(3):561–568. © 2015 by Elsevier Inc. All rights reserved.)

HYDROXYCHLOROQUINE RETINOPATHY IS A WELL-described long-term potential side effect of chronic therapy. Permanent vision loss may occur with development of the characteristic bilateral bull's-eye maculopathy.[1–3] Although hydroxychloroquine has demonstrated a more favorable side effect profile with decreased ocular toxicity compared to chloroquine, the risk for retinopathy is still present, with rates varying from 1% to as high as 7.5% in patients with long-term exposure.[2–9]

In 2011, the American Academy of Ophthalmology (AAO) revised its 2002 guidelines for hydroxychloroquine retinal toxicity screening.[10] The intended goal of the new screening guidelines was to detect functional and anatomic abnormalities related to toxicity at an early stage, with the hope of minimizing irrevocable central blindness. In contradistinction to the 2002 guidelines, the 2011 guidelines recommended subjective testing with a 10-2 Humphrey visual field (HVF) that could no longer be substituted by the previously accepted Amsler grid test.[10–12] An alternatively accepted objective test in the new guidelines includes a multifocal electroretinogram (mfERG). Additional recommended anatomic tests to detect subtle anatomic change include spectral-domain optical coherence tomography (SD OCT) and fundus autofluorescence (FAF).

The guidelines further reiterated specific risk factors associated with toxicity and made screening guidelines accordingly. The designation of high-risk included patients with: (1) cumulative hydroxychloroquine consumption >1 kg; (2) daily dosing >6.5 mg/kg/day of *ideal* body weight; or (3) concomitant renal or liver disease. Additional, albeit less definitive, risk factors included advanced age or comorbid retinal or macular disease. For those without high-risk characteristics, a baseline screening upon initiation of hydroxychloroquine was recommended followed by a 5-year examination-free window. For patients with high risk factors, annual screening was recommended.[10]

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TABLE 1. Hydroxychloroquine Screening Practice Patterns: Patient Demographics

Characteristics	Statistics
Average age (median, mean, range)	56, 55.84, 12–93
Male (n, %)	95, 12.6%
Female (n, %)	661, 87.4%
Diagnosis of patients screened (n, %)	
Rheumatoid arthritis	281, 37.2%
Juvenile rheumatoid arthritis	7, 0.9%
Systemic lupus erythematosus	253, 33.5%
Sjogren syndrome	114, 15.1%
Other[a]	221, 29.23%
Dose of hydroxychloroquine (n, %)	
>400 mg/day	2, 0.26%
400 mg/day	517, 68.4%
201–399 mg/day	29, 3.8%
≤200 mg/day	208, 27.5%
Actual body weight in kg (mean, range)	79.6, 34.9–169.2
Ideal body weight in kg (mean, range)	56.7, 20.2–89.1
Dosing by ideal body weight (n, %)	
Patients receiving <6.5 mg/kg/day	374, 49.5%
Patients receiving ≥6.5 mg/kg/day	382, 50.5%
Duration of hydroxychloroquine treatment	
Mean (y)	6.3
Range (y)	0–46.1
0–5 years (n, %)	402, 53.2%
5–15 years (n, %)	292, 38.6%
15+ years (n, %)	62, 8.2%
Cumulative dose	
Median (grams)	560.8
Mean (grams)	764.6
Range (grams)	0–6735.2
Patients receiving <1 kg lifetime dose (n, %)	553, 73.2%
Patients receiving ≥1 kg lifetime dose (n, %)	203, 26.9%
Comorbid systemic disease (n, %)	
Renal disease	17, 2.3%
Liver disease	60, 7.9%
Risk stratification (n, %)	
High risk[b]	497, 65.7%
Low risk	259, 34.3%

Data based on 756 patients.

[a]Ankylosing spondylitis, arthritis, arthropathy, autoimmune disorder, autoimmune enteropathy, autoinflammatory syndrome, chronic idiopathic urticarial, chronic polychondirits, connective tissue disease (CTD), CREST, Crohn disease, cutaneous vasculitis, dermatomyositis, diffuse CTD, osteoarthritis, fibromyalgia, Kikuchi-Fujimoto syndrome, inflammatory arthritis, inflammatory polyarthropathy, juvenile idiopathic arthritis, Lambert-Eaton myasthenic syndrome, lichen planopilaris, lymphomatoid hyperplasia, mixed CTD, multiple sclerosis, palimdromic rheumatism, paraneoplastic arthritis, pemphigus foliaceous, polymyalgia rheumatica, psoriatic arthropathy, Raynaud syndrome, reactive arthritis, sarcoidosis, scleroderma, seronegative arthritis, seronegative inflammatory arthritis, Still disease, synovitis, systemic sclerosis, ulcerative colitis, undifferentiated CTD, unknown, urticarial vasculitis, Wegener granulomatosis.

[b]>6.5 mg/kg/day dosing per ideal body weight, >1 kg cumulative dose of hydroxychloroquine, or comorbid renal/hepatic toxicity.

Despite the refined guidelines and increased availability of testing, overall adherence to the guidelines, particularly in long-term hydroxychloroquine users, has been reportedly poor. Nika and associates evaluated long-term users of chloroquine and hydroxychloroquine and demonstrated that a third of high-risk patients did not receive appropriate diagnostic testing and just under a third lacked regular eye care.[13] Additionally, Browning showed poor documentation of patient height, weight, daily dose, and cumulative dose that would otherwise be helpful in risk stratification; a reliance on mfERG and SD OCT that was likely responsible for increasing the cost of screening; and the absence of increased toxicity detection since the new recommendations.[7] These studies suggest poor overall compliance and highlight the difficulty of determining the true rate of hydroxychloroquine toxicity.

In this study, we report clinician patterns of hydroxychloroquine screening in a large multispecialty ophthalmology practice. Furthermore, we investigate whether differences in eye care specialization affect choice of screening test and whether or not that correlates with screening guideline compliance.

METHODS

THIS IS AN EVALUATION OF ADHERENCE TO A SCREENING protocol of patients taking hydroxychloroquine between March 11, 2011 (1 month after the 2011 guidelines publication) and September 18, 2014. Waiver of informed consent and waiver of HIPAA authorization were approved by the Cleveland Clinic Institutional Review Board. Inclusion criteria were patients of the Cleveland Clinic Cole Eye Institute who had hydroxychloroquine listed as an active medication in the electronic medical record. Medical records of 881 patients were identified. The initial 881 patients were filtered to 756 patients based on the following exclusion criteria: (1) screening was performed by an outside physician (12 patients, 1.4%); (2) lacked recorded height or weight in the electronic medical record (25 patients, 2.8%); (3) had unavailable hydroxychloroquine start date or dosing (35, 4.0%); and (4) hydroxychloroquine was prescribed for malaria prophylaxis (53, 6.0%). Of the 756 patients, 735 had initial screening encounters and 559 underwent subsequent follow-up screening examinations within the evaluation period. Baseline examination was defined as patients who had been seen for hydroxychloroquine screening within 1 year of starting medication.

Data collected from the electronic medical record included baseline demographic factors (such as height/weight), date hydroxychloroquine was initiated, hydroxychloroquine dose, ancillary tests used, past medical history, pre-existing ophthalmologic disease, examination findings,